Experimental Testicular Cancer containing primarily Squamous Cell Carcinoma

—A comparative investigation of a rat ovarian cancer—

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Summary: A chemical carcinogen, 7, 12 dimethylbenz (α) anthracene, was applied directly to the testis of Wistar rats. After application for ten months, a primary testicular tumor was found in three of nine rats. Histologic examination of the neoplasms indicated that they were primarily squamous cell carcinomas. This is the first report demonstrating induced epidermoid carcinoma in rat testis, although the exact histogenesis remains unknown.

Key Words: 7, 12 dimethylbenz (α) anthracene—rat testicular tumor—squamous cell carcinoma—induced ovarian cancer—histologic origin

Introduction

7, 12 dimethylbenz (α) anthracene (DMBA) is generally regarded as an effective chemical inducer of experimental carcinoma. When implanted directly in a rat ovary, DMBA induced an ovarian adenocarcinoma which was presumably derived from the surface epithelium of the ovary. Due to the morphologic and biologic similarity to the human ovarian tumors, the induced ovarian cancer of the rat has been paid an attention as an expectable model for the common epithelial tumors of the human ovary.

To develop a better understanding of the tumorigenic process caused by DMBA application, rat testis which has the same embryonic origin as the ovary, was also studied. The purpose of this paper is to describe an induced epidermoid carcinoma in rat testes, and to discuss the histogenesis.

Materials and Methods

Male Wistar strain rats, 6 weeks of age, were used in this investigation. DMBA was purchased from Wako Junyaku Co., K.K. in Osaka. Under general anesthesia with ethyl-ether, the left testis of the rat was exposed surgically, and a DMBA impregnated silk suture was inserted into the naked testis with a surgical needle and knotted following the same procedure that was used to induce the rat ovarian cancer. After an experimental period of ten months, the time required for the ovarian cancer induction, the rats were killed and their testes were examined histologically. The tumor tissues were fixed with 10 % formaldehyde, embedded in paraffin and stained with haematoxylin and eosin (HE) for light microscopy.
Results

One of the 10 rats died from an infection 6 days after the carcinogen administration. Testicular tumors were found in 3 of the remaining rats. These testes were enlarged in size to $5.2 \times 3.1 \times 3.1 \text{ cm}$, $4.9 \times 3.1 \times 2.6$ and $4.7 \times 3.4 \times 2.8 \text{ cm}$ in contrast with $2.2 \times 1.1 \times 0.9 \text{ cm}$ in the mean size of the other testes showing normal appearances. The right testis of each rat had a normal size and appearance. The scrota were also intact in each case.

The histology of the DMBA-induced testicular tumor was quite different from the histology of the DMBA-induced ovarian cancer. A typical ovarian tumor is shown in Fig. 1, of the serous type adenocarcinoma. In the testis, the tumor appeared to be intratubular, but the forms were irregular, giant sized and occasionally anastomosed (Fig. 2). Also they did not have a remarkable anaplasia, the tumor cells occurred in the sheet with keratinizing pearl formation and infiltrated in the stroma, indicating well differentiated squamous cell carcinoma. In the fibrous stroma, the efferent tubules were recognized. All three of the induced tumors had similar histological features.

One tumor had the histological characteristics of squamous cell carcinoma, but also had scattered cells with a prominent eosinophilic cytoplasm in the stroma. They could be interstitial cells (Fig. 3). No speriogenic process was observed in the testes that were treated with DMBA.

Fig. 1. A histologic section of a typical ovarian adenocarcinoma induced by DMBA. (HE×100)
Fig. 2. Keratinizing pearl formation in an induced tumor (case 1) with intratubular growth. (HE×100)

Fig. 3. Squamous cell carcinoma in another tumor. Note the interstitial cells in the stroma (right upper corner). (HE×100)
Discussion

DMBA successfully induced ovarian carcinoma in rats with a high incidence. Most of the ovarian tumors (about 80%) were adenocarcinomas, and it is generally accepted that they are derived from the ovarian surface epithelium which receives repetitive minor trauma as a result of ovulation. Epithelial tumors in the testis are very rare in both clinical and experimental settings. The primary histologic origin of testicular tumors is the germ cell which is constantly maturing in the seminiferous tubules. The surface epithelium in the testis is an improbable origin of epithelial tumors, because it is a quiet tissue with no minor trauma or exogenous stimulation equivalent to that which reaches the ovary via the female genital tracts. Both the minor trauma and stimulation supposedly play a significant role in ovarian tumorigenesis.

It is well known that systemic administration of DMBA induces ovarian tumors of the sex-cord stromal category in rodents, after complete destruction of the ova and follicles. The complete eradication of the spermiogenic system also supports this radiomimetic mechanism for DMBA. Because of the carcinogen acts on germ cells, no acceptable experimental evidence for induced germ cell tumors has been presented for DMBA-treatment alone. The germ cells are probably not the tissue of histologic origin for the testicular cancer.

From the intra-tubular growth, it is reasonable to suggest that the epidermoid cancers in the testes arise from a cell lining in the tubular structures, such as the seminiferous tubules or collecting ducts. A metaplastic change from mesothelioma cannot be excluded.

To determine the exact histologic origin of these cancers, more detailed investigations are required.

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References